TO WHITE OPENPTO 2 -8 JUNI 2002

U S DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE ATTORNEY 'S DOCKET NUMBER FORM PTO-1390 S04P02US TRANSMITTAL LETTER TO THE UNITED STATES US APPLICATION NO (If known, see 37 CFR 1 5 DESIGNATED/ELECTED OFFICE (DO/EO/US) 10/049247 CONCERNING A FILING UNDER 35 U.S.C. 371 PRIORITY DATE CLAIMED INTERNATIONAL FILING DATE INTERNATIONAL APPLICATION NO. PCT/DE00/02472 7/27/1999 7/27/2000 Method and Particular Device for Measuring Cardiomagnetic Fields Biomagnetic and in TITLE OF INVENTION APPLICANT(S) FOR DO/EO/US Fritz Steinberg and Volodymyr Sosnitzky Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information: 1. X This is a FIRST submission of items concerning a filing under 35 U.S.C. 371. This is a SECOND or SUBSEQUENT submission of items concerning a filing under 35 U.S.C. 371. This is an express request to begin national examination procedures (35 U.S.C. 371(f)). The submission must include items (5), (6), (9) and (21) indicated below. The US has been elected by the expiration of 19 months from the priority date (Article 31). A copy of the International Application as filed (35 U.S.C. 371(c)(2)) as corrected under Rule 91 is attached hereto (required only if not communicated by the International Bureau). has been communicated by the International Bureau. is not required, as the application was filed in the United States Receiving Office (RO/US). An English language translation of the International Application as filed (35 U.S.C. 371(c)(2)). and corrected under Rule 91 6. X is attached hereto. has been previously submitted under 35 U.S.C. 154(d)(4). Amendments to the claims of the International Aplication under PCT Article 19 (35 U.S.C. 371(c)(3)) are attached hereto (required only if not communicated by the International Bureau). have been communicated by the International Bureau. have not been made; however, the time limit for making such amendments has NOT expired. have not been made and will not be made. 8. An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371 (c)(3)). An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)). 10. An English lanugage translation of the annexes of the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)). Items 11 to 20 below concern document(s) or information included: An Information Disclosure Statement under 37 CFR 1.97 and 1.98. An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included. 12. A FIRST preliminary amendment. 13.X A SECOND or SUBSEQUENT preliminary amendment. A substitute specification. A change of power of attorney and/or address letter. A computer-readable form of the sequence listing in accordance with PCT Rule 13ter.2 and 35 U.S.C. 1.821 - 1.825. A second copy of the published international application under 35 U.S.C. 154(d)(4). 18. A second copy of the English language translation of the international application under 35 U.S.C. 154(d)(4). 19. "Express Mail" Label # EU 091 934 518 US - I hereby 20. X Other items or information: certify that this paper or fee is being deposited with the Application Data Sheet USPS "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on 1/28/2002, and is addressed to the Assistant Commissioner for Patents, Washington, D.C. Gudrun E. Huckett, Patent Agent 20231.

U.S. APPLICATION NO. (I known, see 37 CFR) 57 INTERNATIONAL APPLICATION NO. PCT/DE00/02472 ATTORNEY: DOCKET NUMBER S04P02US

21. A The following fees are submitted:

BASIC NATIONAL FEE (37 CFR 1.492 (a) (1) - (5)):

Neither international preliminary examination fee (37 CFR 1.482)
nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO and International Search Papert not prepared by the FPO or IPPO

	UNDERV			5041020		
21. The following fees are submitted:				CALCULATIONS	PTO USE ONLY	
T	FEE (37 CFR 1.492 (a)					
nor international se	al preliminary examination earch fee (37 CFR 1.445) earch Report not prepare					
		7 CFR 1.482) not paid to pared by the EPO or JPO				
International prelim	ninary examination fee (3	7 CFR 1.482) not paid to (2)) paid to USPTO	USPTO			
		7 CFR 1.482) paid to US				
but all claims did no	ot satisfy provisions of PC					
	ninary examination fee (3 fied provisions of PCT A		<del></del>			
ENTE	R APPROPRIATE	\$ 890.00				
Surcharge of \$130.0 months from the ear	0 for furnishing the oath liest claimed priority date	\$ 130.00				
CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE	\$		
Total claims	55 - 20 =	35	x \$18.00	\$ 630.00		
Independent claims	2 - 3 =	0	x \$84.00	\$ 0.00		
MULTIPLE DEPEN	DENT CLAIM(S) (if app	<del> </del>	+ \$280.00 LATIONS =	\$ 1650.00	1	
Applicant claim	TOTAL O	\$ 1650.00	<u> </u>			
Applicant claim are reduced by		\$ 825.00				
			$\begin{array}{c c} \mathbf{BTOTAL} &= \\ \mathbf{an} & 20 & 30 \end{array}$	\$ 825.00		
Processing fee of \$1, months from the ear	30.00 for furnishing the I liest claimed priority date	\$				
		\$ 825.00				
		7 CFR 1.21(h)). The assist 7 CFR 3.28, 3.31). <b>\$40.</b> 0		\$		
		TOTAL FEES EI	NCLOSED =	\$ 825.00		
				Amount to be refunded:	\$	
				charged:	\$	
a. X A check in the amount of \$ 825.00 to cover the above fees is enclosed. check # 1334						
b. Please charge my Deposit Account No in the amount of \$ to cover the above fees.  A duplicate copy of this sheet is enclosed.						
c. X The Commoverpayme	issioner is hereby authori nt to Deposit Account No	zed to charge any additio 50–1199 . A duplic	nal fees which may b ate copy of this sheet	e required, or credit and is enclosed.	ny	
		rd. WARNING: Information this form. Provide co				
			-			
		under 37 CFR 1.494 or 1 to restore the application			ve (37 CFR	
SEND ALL CORRESPO	ONDENCE TO		,	0 11	2	
			SIGNATIO	idnu E. Hu	cicos	
	Huckett, Patent Ag	drun E. Huckett				
P.O. Box 3 Albuquerqu	187 ie, NM 87190-3187	5,747				
				ATION NUMBER		
				/28/2002		

1049247 JC13 Rec'd PCT/PTO 28 JAN 2002

#### IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

"Express Mail" Mailing Label Number EU091934518US Date of Deposit January 28, 2002

I hereby certify that this paper or fee is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231.

Gudrun E. Huckett, Patent Agent

Applicant:

Fritz Steinberg, et al.

Serial No:

not yet known (based on PCT/DE00/02472)

International Filing Date: 7/27/2000

U.S. Filed:

1/28/2002

Title:

Method and Device for Measuring Biomagnetic and in

Particular Cardiomagnetic Fields

#### **Assistant Commissioner for Patents**

Washington, D.C. 20231

#### PRELIMINARY AMENDMENT

Prior to the first office action, please amend the instant application as follows:

#### IN THE SPECIFICATION:

Please substitute the attached clean copies of the amended paragraphs of page 1. lines 1-11; page 4, lines 1-4; page 10, lines 18-26; page 12, lines 3-17 for the corresponding paragraphs of the literal translation as filed. A marked-up version of the amended paragraphs of the pages 1, 4, 10, 12 with all the changes shown is also attached. IN THE CLAIMS:

Claims 1 through 44 are cancelled. Please add the attached new claims 45-99 to

the specification.

#### **IN THE ABSTRACT:**

Please add the attached Abstract of the Disclosure to the specification.

#### **REMARKS**

Claims 1-44 have been cancelled and replaced with new claims 45-99 drafted in proper U.S. format. Proper headings according to the guidelines for drafting a nonprovisional patent application under 35 U.S.C. 111(a) have been added. A proper Abstract of the Disclosure has been added to the specification.

In view of the foregoing, it is submitted that this application is now in condition for allowance and such allowance is respectfully solicited.

Authorization is herewith given to charge any fees or any shortages in any fees required during prosecution of this application and not paid by other means to Patent and Trademark Office deposit account 50-1199.

Respectfully submitted on January 28, 2002

Gudrun E. Huckett, Ph.D. Registration No. 35,747

Gudrun E. Huckett, Patent Agent P.O. Box. 3187

Gudnu F. Hucliets

Albuquerque, NM 87190-3187

Telephone: (505) 266-2138 Facsimile: (505) 266-2138

GEH

Encl.: - new claims 45-99;

- amended paragraphs of pages 1, 4, 10, 12 (clean copies and marked-up copies);

- Abstract

#### **NEW CLAIMS 45-99**

- 45. A device for measuring biomagnetic fields, comprising at least one superconducting quantum interference device (SQUID), wherein the SQUID is a SQUID with hysteresic voltage-current characteristic, and further comprising means for operating the SQUID in relaxation oscillation mode (RO mode).
- 46. The device according to claim 45, wherein the SQUID is a direct-current SQUID (DC SQUID).
- 47. The device according to claim 45, wherein the SQUID has at least two Josephson junctions (tunnel connections).
- 48. The device according to claim 47, wherein the at least two Josephson junctions are internally unshunted and are connected by a line with one another.
- 49. The device according to claim 47, wherein the at least two Josephson junctions have such a capacitance C that the voltage-current characteristic of the SQUID has hysteresis.
- 50. The device according to claim 49, wherein the means for operating the SQUID in relaxation oscillation mode comprise a resistor R and an inductive resistor L series-connected to one another.
- 51. The device according to claim 50, wherein the SQUID has two areal superconducting areas connected to one another by the at least two Josephson junctions, wherein the two superconducting areas, in addition to the connection via the Josephson junctions, are connected with one another by the resistor R and the inductive resistor L.

- 52. The device according to claim 51, wherein the greater one of the two superconducting areas has an edge length between 1.5 mm and 2.5 mm.
- 53. The device according to claim 51, wherein a surface area enclosed by the two superconducting areas of the SQUID is between 1,200  $\mu$ m<sup>2</sup> and 2,000  $\mu$ m<sup>2</sup>.
- 54. The device according to claim 45, wherein the SQUID is a low-temperature SQUID.
- 55. The device according to claim 45, wherein the SQUID is a SQUID of a washer configuration.
- 56. The device according to claim 45, further comprising an input coil and at least one antenna, wherein the SQUID is coupled inductively via the input coil to the at least one antenna.
- 57. The device according to claim 56, wherein the at least one antenna is comprised of superconducting material and has at least one first coil (pickup coil) for inductive detection of a magnetic field and a second coil (input coil).
- 58. The device according to claim 56, wherein the at least one antenna is a gradiometer antenna having at least one bucking coil in addition to the pickup coil.
- 59. The device according to claim 58, wherein the gradiometer antenna is a symmetric axial second-order gradiometer antenna having three bucking coils.
- 60. The device according to claim 58, wherein the gradiometer antenna has a baseline of between 5 and 7 cm.
- 61. The device according to claim 58, comprising means for mechanically compensating (balancing) the gradiometer.

- 62. The device according to claim 61, wherein the means for mechanically compensating comprise a mechanism for exact positioning of one or several superconducting objects in the vicinity of at least one of the pickup and bucking coils.
- 63. The device according to claim 58, wherein the diameter of the pickup coil and of the at least one present bucking coil is between 1.5 cm and 2.9 cm.
- 64. The device according to claim 58, wherein the at least one bucking coil comprises only one winding.
- 65. The device according to claim 57, wherein the diameter of the pickup coil is between 1.5 cm and 2.9 cm.
- 66. The device according to claim 57, wherein the pickup coil comprises only one winding.
  - 67. The device according to claim 56, wherein the antenna is comprised of wire.
- 68. The device according to claim 67, wherein the antenna is comprised of niobium wire or niobium nitrate wire having a diameter between approximately 30  $\mu$ m and 60  $\mu$ m.
- 69. The device according to claim 56, wherein the input coil has approximately 20 to 40 windings.
- 70. The device according to claim 56, comprising a lens for bundling the magnetic field lines arranged between the input coil and the SQUID.
- 71. The device according to claim 70, wherein the lens is a thin foil of superconducting material.
  - 72. The device according to claim 45, comprising a Dewar container, wherein the

SQUID is arranged in the Dewar container.

- 73. The device according to claim 72, further comprising an input coil and at least one antenna, wherein the SQUID is coupled inductively via the input coil to the at least one antenna, wherein the at least one antenna is comprised of superconducting material and has at least one first coil (pickup coil) for inductive detection of a magnetic field and a second coil (input coil), and wherein the Dewar container with exception of an area underneath the pickup coil is provided with a magnetic shielding.
- 74. The device according to claim 73, wherein the magnetic shielding is comprised of aluminum foil.
- 75. The device according to claim 74, wherein the Dewar container is configured such that a spacing between a bottom side of the pickup coil facing the Dewar container and the outer side of the container is between approximately 3 mm and approximately 10 mm.
- 76. The device according to claim 73, further comprising a magnetically shielded housing surrounding the Dewar container and sensitive parts of an electronic device required for operating the SQUID, wherein the housing has an opening for the area of the Dewar container containing the pickup coil.
- 77. The device according to claim 76, wherein the housing is lined with aluminum foil.
- 78. The device according to claim 72, wherein the Dewar container has a cooling medium volume in the range of between 2.5 I and 10 I.
  - 79. The device according to claim 45 for detecting cardiomagnetic fields, having

one or several SQUIDs each having an antenna.

- 80. The device according to claim 79, wherein four to nine SQUIDs are provided.
- 81. The device according to claim 45, having at least one pickup coil for determining biomagnetic fields, further comprising a movable table for positioning an object to be examined relative to the at least one pickup coil.
- 82. The device according to claim 81, wherein the table is comprised of nonconducting material selected from the group consisting of wood and plastic material.
- 83. The device according to claim 81, further comprising a locking and guiding mechanism for moving the table along predetermined paths and for locking the table in certain positions.
- 84. The device according to claim 81, further comprising means for automatically positioning the table relative to the at lest one pickup coil.
- 85. The device according to claim 84, wherein the means for automatically positioning the table relative to the at least one pickup coil are selected from the group consisting of hydraulic means, mechanical means, and hydraulic-mechanical means.
- 86. The device according to claim 85, wherein the means for automatically positioning comprise one or several spindle drives.
- 87. The device according to claim 81, wherein the table and the at least one pickup coil are configured such that, when measuring magnetic fields at different locations of the object, the object is moved relative to the at least one pickup coil by moving the table while maintaining the absolute position of the at least one pickup coil.
  - 88. The device according to claim 45, comprising a measuring or evaluation

electronic device for automatically considering disturbances that can be derived from the periodic current-flux characteristics for switched-off feedback in order to automatically discard measured values recorded during occurrence of disturbances.

- 89. A method for measuring biomagnetic fields with at least one antenna of superconducting material arranged in a Dewar container, wherein the antenna comprises at least one first coil (pickup coil) for inductive detection of a magnetic field and a second coil (input coil), and with a SQUID inductively coupled to the antenna in the Dewar container via the input coil, the method comprising the step of operating the SQUID in relaxation oscillation mode.
- 90. The method according to claim 89, wherein an internally unshunted SQUID with hysteresic voltage-current characteristic and with two areal superconducting areas connected to one another by two Josephson junctions (tunnel connections), which are externally connected to one another by means of a resistor R and an inductive resistor L series-connected to the resistor R, is used, comprising the step of applying a bias voltage to the SQUID such that the relaxation oscillation mode is realized.
- 91. The method according to claim 89, further comprising the step of obtaining, before measuring biomagnetic fields, information in regard to noise present at the installation site of the device from periodic current-flux characteristics of the SQUID with the feedback being switched off.
- 92. The method according to claim 89, further comprising the step of testing the SQUID, before measuring biomagnetic fields, in regard to proper function and quality by observing periodic current-flux characteristic of the SQUID with the feedback being

switched off.

- 93. The method according to claim 89, further comprising the step of automatically taken into consideration certain disturbances of the measurement by automatically discarding measured values recorded at the time of occurrence of disturbances.
- 94. The method according to claim 89, wherein the antenna is configured as a gradiometer with at least one bucking coil and wherein the gradiometer is mechanically compensated (balanced).
- 95. The method according to claim 94, comprising the step of positioning one or several superconducting objects in the vicinity of the pickup and bucking coils.
- 96. The method according to claim 89, wherein the object to be examined is moved into one or several different positions relative to the at least one pickup coil.
- 97. The method according to claim 96, wherein the absolute position of the at least one pickup coil is not changed when performing the relative movement of the object to be examined.
- 98. The method according to claim 96, wherein for detecting cardiomagnetic fields, the fields are measured on 36 points of a rectangular grid at a 4 cm spacing, respectively, to the neighboring points.
- 99. The method according to claim 89 for detecting cardiomagnetic fields, wherein rooms in which the method is performed require no shielding against external electromagnetic fields.

#### **CLEAN COPY OF PAGE 1, LINES 1-11**

# Method and Device for Measuring Biomagnetic and in Particular Cardiomagnetic Fields

#### BACKGROUND OF THE INVENTION

#### 1. Field of the Invention

The invention relates to a method and a device for measuring biomagnetic, in particular, cardiomagnetic, fields by means of at least one superconducting quantum interference device (SQUID).

# 2. Description of the Related Art

Such methods and devices are known in various forms (see, for example, H. Weinstock (Ed.): "SQUID sensors-and fundamentals, fabrication and applications", Kluwer Academic Publishers, 1996). They comprise generally at least one antenna of superconducting material, wherein the antenna has at least one first coil for inductive detection of a magnetic field and a second coil and, in general, is coupled inductively with the SQUID.

# **CLEAN COPY OF PAGE 4, LINES 1-4**

#### SUMMARY OF THE INVENTION

Based on this, the invention has the object to provide a method and a device of the aforementioned kind which enable the measurement of biomagnetic signals with especially simple means, in particular, also in unshielded rooms, and thus in a cost-effective way.

# **CLEAN COPY OF PAGE 10, LINES 18-26**

12 T 4

Preferably, the method is performed such that an internal unshunted SQUID with hysteresic voltage-current characteristic and two areal superconducting areas connected to one another by two Josephson junctions (tunnel connections) and connected with one another externally by a resistor R and an inductive resistor L, series-connected to the resistor R, are employed and that a bias voltage is supplied to the SQUID such that the relaxation oscillation mode is realized.

#### BRIFF DESCRIPTION OF THE DRAWINGS

Further details and advantages of the invention result from the following purely exemplary and non-limiting description of a few embodiments in connection with the drawing, in which:

# **CLEAN COPY OF PAGE 12, LINES 3-17**

Fig. 10 shows the RO frequency dependency of magnetic flux MF wherein the line 1 shows the course without and the line 2 the course with additional positive feedback (APF); 2) and wherein for clarification the circuit diagram of the SQUID APF circuit is inserted into the Figure.

#### **DESCRIPTION OF PREFERRED EMBODIMENTS**

Fig. 1 shows a magnetograph comprising a Dewar container D in which the actual measuring device is arranged and which is suspended from a gantry G. The magnetograph comprises furthermore a frame F with a movable support S, with which the patient P to be examined can be positioned underneath the measuring device; a comparison EKG E; a control unit C; a personal computer PC; and a connecting cable CC for connecting the measuring device arranged in the container D with the control unit C.

The gantry G and the movable support S together make possible the positioning of the patient P relative to the measuring device in the desired way. The gantry, support and frame are made of non-magnetic material such as wood or Textolite.

# **MARKED-UP VERSION OF PAGE 1, LINES 1-11**

# Method and Device for Measuring Biomagnetic and in Particular Cardiomagnetic Fields

#### BACKGROUND OF THE INVENTION

# 1. Field of the Invention

The invention relates to a method and a device for measuring biomagnetic, in particular, cardiomagnetic, fields by means of at least one superconducting quantum interference device (SQUID).

# Description of the Related Art

Such methods and devices are known in various forms (see, for example, H. Weinstock (Ed.): "SQUID sensors-and fundamentals, fabrication and applications", Kluwer Academic Publishers, 1996). They comprise generally at least one antenna of superconducting material, wherein the antenna has at least one first coil for inductive detection of a magnetic field and a second coil and, in general, is coupled inductively with the SQUID.

# MARKED-UP VERSION OF PAGE 4, LINES 1-4

# **SUMMARY OF THE INVENTION**

Based on this, the invention has the object to provide a method and a device of the aforementioned kind which enable the measurement of biomagnetic signals with especially simple means, in particular, also in unshielded rooms, and thus in a cost-effective way.

#### MARKED-UP VERSION OF PAGE 10, LINES 18-26

Preferably, the method is performed such that an internal unshunted SQUID with hysteresic voltage-current characteristic and two areal superconducting areas connected to one another by two Josephson junctions (tunnel connections) and connected with one another externally by a resistor R and an inductive resistor L, series-connected to the resistor R, are employed and that a bias voltage is supplied to the SQUID such that the relaxation oscillation mode is realized.

#### **BRIEF DESCRIPTION OF THE DRAWINGS**

Further details and advantages of the invention result from the following purely exemplary and non-limiting description of a few embodiments in connection with the drawing, in which:

# **MARKED-UP VERSION OF PAGE 12, LINES 3-17**

Fig. 10 shows the RO frequency dependency of magnetic flux MF wherein the line 1 shows the course without and the line 2 the course with additional positive feedback (APF); 2) and wherein for clarification the circuit diagram of the SQUID APF circuit is inserted into the Figure.

#### **DESCRIPTION OF PREFERRED EMBODIMENTS**

Fig. 1 shows a magnetograph comprising a Dewar container  $\frac{1}{D}$  in which the actual measuring device is arranged and which is suspended from a gantry  $\frac{2}{D}$ . The magnetograph comprises furthermore a frame  $\frac{3}{D}$  with a movable support  $\frac{4}{D}$ , with which the patient  $\frac{5}{D}$  to be examined can be positioned underneath the measuring device; a comparison EKG  $\frac{6}{D}$ ; a control unit  $\frac{7}{D}$ ; a personal computer  $\frac{8}{D}$  PC; and a connecting cable  $\frac{9}{D}$  CC for connecting the measuring device arranged in the container  $\frac{4}{D}$  with the control unit  $\frac{7}{D}$ .

The gantry  $\underline{2}$   $\underline{G}$  and the movable support  $\underline{4}$   $\underline{S}$  together make possible the positioning of the patient  $\underline{5}$   $\underline{P}$  relative to the measuring device in the desired way. The gantry, support and frame are made of non-magnetic material such as wood or Textolite.

#### ABSTRACT OF THE DISCLOSURE

A device for measuring biomagnetic fields is provided with at least one superconducting quantum interference device (SQUID). The SQUID is a SQUID with hysteresic voltage-current characteristic. The SQUID is operated in a relaxation oscillation mode (RO mode) by providing a resistor and an inductive resistor series-connected to one another. The SQUID has two areal superconducting areas connected to one another by Josephson junctions, wherein the two superconducting areas, in addition to the connection via the Josephson junctions, are connected with one another by the resistor and the inductive resistor. This configuration allows use of the device in rooms that are not shielded against external electromagnetic fields.

7 3. 3. 3. 3. 3. 3.

5

10

15

20

25

# Method and Device for Measuring Biomagnetic and in Particular Cardiomagnetic Fields

The invention relates to a method and a device for measuring biomagnetic, in particular, cardiomagnetic, fields by means of at least one superconducting quantum interference device (SQUID).

Such methods and devices are known in various forms (see, for example, H. Weinstock (Ed.): "SQUID sensors-and fundamentals, fabrication and applications", Kluwer Academic Publishers, 1996). They comprise generally at least one antenna of superconducting material, wherein the antenna has at least one first coil for inductive detection of a magnetic field and a second coil and, in general, is coupled inductively with the SQUID.

In this connection, the term "antenna" refers to a conductor loop bent generally of a wire with at least two coils comprised of one or several windings, respectively, wherein in one of the coils (the so-called pickup coil) a current is induced by a magnetic field which then can be imparted by means of the second coil (the so-called input coil) inductively onto a superconducting quantum interference device which results in measurable physical processes. In this type of measurement of magnetic fields, the Josephson effect (Cooper pairs may tunnel through a non-superconducting thin connecting area - a so-called Josephson junction - between two superconducting areas) as well as the fact that the magnetic flux through superconducting coils is quantized are utilized.

For quite some time now, research groups throughout the world have worked on the measurement of biomagnetic fields which, as has been recognized, provide important information in regard to pathological anomalies of very different kinds. For example, since the end of the 1960s experiments have been carried out with SQUIDS of most different configurations in order to measure smallest magnetic

fields caused by brain waves and cardiac waves. Some of these measurements have electrical analogs (for example, the magnetocardiography with electrocardiography and magnetoencephalography with electroencephalography) but others do not (for example, the non-invasive measurement of magnetic susceptibility of tissues and organs or the measurement of magnetic "direct-current fields" which are generated by inhaled, injected or orally taken magnetic materials).

5

10

15

20

25

In this connection, it has been proven by a plurality of studies (compare, for example, W. Andrä & H. Nowak (Eds.): "Magnetism in Medicine", Wiley-VCH, 1998, 139ff; or Hailer et al.: "Die Anwendung des Biomagnetismus in der Kardiologie" (Use of Biomagnetism in Cardiology) in: Prakt. Kardiol., Vol. 15, 1995, pp. 90-103; each with additional references) that the magnetocardiography (MCG) by means of SQUID sensors is an important auxiliary means in the diagnosis and therapy control, in particular, also in the risk stratification and early detection of a number of heart diseases and heart malfunctions. For example, by means of purely visual differences in the magnetic field maps (MFM) of healthy and diseased hearts, certain diseases and risks can be detected and early preventive measures can thus be initiated.

Since moreover only the magnetic fields resulting from the body's own activities are measured, the measurement of biomagnetic fields - in contrast to methods such as ultrasound or magnetic resonance imaging tomography in which the body parts to be examined are subjected to external fields or sound waves - is indeed absolutely non-invasive and thus without any disadvantageous effect on the examined body part. Moreover, the magnetic fields can be measured completely contact-free so that the patient, who in most cases is already psychologically stressed because of his disease, must not be "wired" to a device that is possibly threatening to him.

A further great advantage of the measurement of biomagnetic fields resides in the fact that the magnetic permeability of almost all materials is substantially equal to

1 so that, for example, magnetic fields generated by the heart activity can penetrate, almost uncorrupted and practically without loss, bone, soft tissue, and air to reach the corresponding sensors. On the other hand, the electrical conductivity varies greatly. Therefore, it is comparatively difficult to interpret waves that can be measured by EKG relative to their point of origin since, on their path to the measuring electrodes, they move always on those conductive paths which provide the maximum conductivity and thus the minimum electrical resistance.

5

10

15

20

25

Despite the recognized great advantages of the measurement of biomagnetic fields and, in particular, of the MCG, especially for early detection and prenatal diagnostic, and despite the fact that already for approximately 30 years experiments with respect to the detection of biomagnetic fields by means of SQUID sensors have been undertaken, the measurement of biomagnetic fields has not yet developed into a standard examination method.

This is, on the one hand, the result of the very high acquisition and maintenance costs of such known devices which, partially, provide acceptable measured data only in magnetically shielded rooms, wherein already the construction of such a magnetically shielded room requires great expenditures. On the other hand, the evaluation of the signals detected with the known devices requires a complex and partially very time-consuming after-processing which can be performed only by specialists.

The conventionally employed magnetometers are based on direct-current SQUIDs (DC SQUIDs) with a ring with two Josephson junctions and a direct-current bias voltage wherein these SQUIDs have a hysteresis-free voltage-current characteristic. This requires a so-called shunting of the Josephson junctions with high capacitance which, in turn, results in a comparatively slow analog electronic device which operates with signals in the microvolt range and requires, in particular, for measuring low-frequency fields, a complex shielding and filtration.

Based on this, the invention has the object to provide a method and a device of the aforementioned kind which enable the measurement of biomagnetic signals with especially simple means, in particular, also in unshielded rooms, and thus in a cost-effective way.

The object is solved, on the one hand, by a device of the aforementioned kind wherein the SQUID is a SQUID with hysteresic voltage-current characteristic and wherein means for operating the SQUID in the relaxation-oscillation mode (RO mode) are provided.

5

10

15

20

25

The invention is thus based on the principle of moving from an analog operation mode into a pulsed mode which has a series of advantages and, in particular, makes it possible to measure smallest magnetic fields also in rooms that are not shielded, primarily also in rooms in the clinical environment where, as a result of the plurality of electrical devices operated nowadays, a particularly strong magnetic noise is present. This is all the more astonishing when considering that the magnetic fields generated by heart activity are within the magnitude of only  $10^{-10}$  Tesla and less while the magnetic field which is caused by a car passing by even at a distance of 50 m still has a strength of  $10^{-8}$  up to  $10^{-9}$  Tesla and a magnetic field generated by a battery-operated tool, for example, a battery-operated screwdriver, even at a distance of 5 m still has a strength of  $10^{-9}$  to  $10^{-10}$  Tesla (compare, for example, J. Vrba: "SQUID Gradiometers in Real Environments"; in H. Weinstock (Ed.): "SQUID Sensors - Fundamentals, Fabrication and Applications", Kluwer Academic Publishers, 1996).

The device is suitable for measurement of very different magnetic fields, in particular, for the magnetocardiography, but also for very different other biomagnetic examinations such as, for example, measurements of the magnetic susceptibility of the liver.

An advantage of the operation in the RO mode is that the important information in regard to the magnetic flux received by the antenna is no longer contained in the noise-sensitive amplitude height of the voltage signals tapped on the SQUID, as is known in the art, but in the frequency of these signals and is thus obtainable substantially simpler and faster, additionally with greater resistance to ambient noise. The entire electronic measuring device can be simplified in comparison to the known devices operating the SQUIDs in analog mode and can thus be embodied less expensively.

5

10

15

20

25

A further advantage of the operation in the RO mode is that, simply by viewing (for switched-off feedback) the periodic current-flux characteristic after installing the device, important information in regard to the noise present at the installation site, in particular, information in regard to cause of the noise, can be obtained; since certain noise sources have a characteristic in typical causes, it is easy to undertake corresponding active or passive countermeasures. When, for example, the regular startup of an elevator motor generates a disturbance field, an electronic measuring or evaluation device can take this into consideration in various ways and, for example, can automatically discard the values measured at the time of switching on the motor. Also, the characteristic shows whether a certain high-frequency noise has external causes or whether the SQUID is possibly defective or of low quality.

A further great advantage of the operation in the RO mode (pulsed operation) is that the voltage-current characteristic of the SQUID becomes insensitive relative to distortions which, in the analog mode, occur as a result of the resonance between the SQUID and the input coil, the SQUID and a feedback coil, and as a result of asymmetries of the superconducting areas and the Josephson junctions. Moreover, the modulation-demodulation method comprising modulation of the magnetic feedback field and required in the known devices for reducing the so-called "1/f" or "flicker" noise is no longer needed because in the RO mode the bias current of the SQUIDs is modulated.

Preferably, the SQUID is an internally unshunted direct-current SQUID (DC SQUID) with at least two Josephson junctions (tunnel connections) which are connected to one another by a line and are not - in contrast to the prior art - bridged by shunts integrated into the component.

Preferably, the means for operating the SQUID in the relaxation oscillation mode have a resistor R and an inductive resistor L, which is series-connected with the resistor R, via which the two superconducting areas are connected to one another, in addition to the connection via the Josephson junctions.

5

10

15

20

25

Preferably, the SQUID is a low-temperature SQUID, i.e., a SQUID whose superconducting properties occur only at very low temperatures, for example, the temperature of liquid helium. In principle, it is also possible to produce SQUIDs of such materials whose superconducting properties occur already at temperatures considerably higher than the temperature of liquid helium, which can bring about advantages with respect to the operating costs; however, the so-called intrinsic noise of such high-temperature SQUIDs is significantly higher than that of low-temperature SQUIDs. The minimally higher operating costs of low-temperature SQUIDs are more than compensated by the measuring-technological advantages, in particular, the simpler signal filtration.

SQUIDs of different spatial configuration can be used. However, it was found to be advantageous when the surface area enclosed by the two superconducting areas of the SQUID is between 1,200 and 2,000  $\mu m^2$ , preferably approximately 1,600  $\mu m^2$ . Particularly well suited are SQUIDs of the so-called washer type (see, in particular, Fig. 5), especially those in which the greater of the two superconducting areas has an edge length between 1.5 and 2.5 mm, preferably of approximately 2 mm.

A device provides very good results already when the antenna together with the SQUID forms a simple magnetometer. The results can be improved even further,

particularly in environments with great magnetic noise, when the antenna forms together with the SQUID a gradiometer wherein, in particular, the configuration as a symmetrical axial second-order gradiometer has been proven to be very advantageous. In such gradiometers the sensitivity relative to magnetic fields drops with the fifth power of the spacing of the sources of the fields to the pickup coil when this spacing is considerably greater than the so-called baseline (the spacing between the pickup coil and the first bucking coil, i.e., the first differentiation coil wound counter to the pickup coil) of the gradiometer. In connection with the measurements on the human body it was found to be advantageous when the baseline is between 5 and 7 cm, preferably approximately 6 cm wherein the diameter of the pickup coils in the case of a magnetometer as well as in the case of a gradiometer and the diameter of the bucking coil(s) present within a gradiometer is between 1.5 and 2.9 cm, preferably approximately 2.2 cm. As a material for manufacturing the antenna niobium wire or niobium nitrate wire with a diameter between approximately 30 and 60 µm was found to be beneficial.

5

10

15

20

25

The pickup coil and the optionally present bucking coils can have several windings, respectively. Preferably, they have only one winding, respectively, such that the inductivity is low and the input coil must have only a few, approximately 20 to 40, windings in order to transfer the current in the desired way inductively onto the SQUID. In this connection, between the input coil and the SQUID a lens, in particular, in the form of a thin foil of a superconducting material, can be provided for focusing magnetic field lines.

When instead of a magnetometer advantageously a gradiometer is used, it must be adjusted as a result of always present deviations from the ideal state (identically sized, uniformly shaped, exactly parallel coils) wherein the deviations are compensated as much as possible. This is referred to usually as "balancing" of the gradiometer. For balancing, different methods are known. As a result of their simplicity, means for a mechanical balancing of the gradiometer, in particular, a

mechanism for exact positioning one or several superconducting objects in the vicinity of the pickup and bucking coils, have proven to be especially successful.

The device, as mentioned, can also be used in unshielded rooms. However, in this connection it is expedient to provide at least the Dewar container, with the exception of an area below the pickup coil, with a magnetic shielding, for example, to line it with aluminum foil. Preferably, a magnetically shielded housing, preferably lined with aluminum foil, is also provided which surrounds the Dewar container and the important sensitive parts of the electronic device required for operating the SQUID and has an opening for the area of the Dewar container in which the pickup coil is arranged.

5

10

15

20

25

The known devices, in particular, for recording cardiomagnetic fields have usually a plurality (in general between 35 and up to 60) antennae and SQUIDs coupled therewith. Also, the printed prior art (compare for example, W. Andrä & H. Nowak (Eds.): "Magnetism in Medicine", Wiley-VCH, 1998) describes these so-called multichannel systems as the most promising systems. The advantage of such systems is that the devices can theoretically scan in the shortest period of time a spatial area, for example, encompassing the entire heart. The great disadvantage of such systems is that the electronic measuring and evaluation device is so complex that, when an error occurs, the localization thereof is difficult and time-consuming. Such systems can thus be operated only by a few specialists and are therefore not widely used in clinical application.

In a preferred embodiment of the invention, in particular, for determining cardiomagnetic fields, it is instead provided that the device has only one or a few, preferably between four to nine, antennae with one SQUID each. This has a series of advantages. For example, the electronic measuring and evaluation device is significantly simplified relative to the known devices and the Dewar container can be sized substantially smaller than in the known devices.

While one device of a well-known manufacturer has a container with a cooling medium volume of 25 liters, where each day approximately 5.2 liters of liquid helium escape, the Dewar container for the device according to the invention can be sized such that it has only a cooling medium volume in the range of a few liters, in particular, between 2.5 and 10 liters. For example, in a device according to the invention for recording cardiomagnetic fields a Dewar container with a volume of 6 I is provided from which each day approximately 1.2 I will escape; in consideration of the significant costs of liquid helium, this results in significantly reduced maintenance costs.

5

10

15

20

25

When only a few antennae are provided this has also the advantage that the coils of each antenna can be made larger. Accordingly, the pickup coils for known multichannel devices have diameters between 0.5 to 1.0 cm while the coil diameter according to the invention is preferably between 1.5 and 2.9 cm, in particular approximately 2.2 cm.

In order to simplify the evaluation of the detected signals even further, according to one advantageous embodiment, in particular, for detecting cardiomagnetic fields, a movable table for positioning an object to be examined relative to the pickup coil(s) is provided. It was found that the noise at one and the same location in a space over the course of the typical measuring intervals is relatively uniform while already a few centimeters away from it a noise can be measured that is also uniform but, with respect to its structure, is considerably different. When the measurements are carried out only at one or a few locations, the filter adjustments can stay the same for different parts of the object measured sequentially at the respective location. As an example, a, for example, rectangular grid with, for example, 4 cm spacing, respectively, to the neighboring points to be measured. If these 36 points were measured with a single channel system (with only one antenna and one SQUID) and if the antenna for this purpose were moved instead of the object to be examined, the recorded 36 measurement series would have to be filtered with

individual new adjustments. If instead the object to be examined is moved and the antenna remains stationary, the filters must be adjusted only once.

The table is comprised preferably of non-magnetic and non-conducting materials such as wood and/or plastic materials. The table can be moved by hand for which purpose a locking and guiding mechanism for moving the table along predetermined paths and securing the table in certain positions can be provided. With greater expenditure it is also possible to position the table automatically relative to the pickup coil(s) wherein, however, care must be taken that the corresponding mechanisms and drives do not represent source of disturbance for the sensitive measuring device.

5

10

15

20

25

The aforementioned object with respect to the method is solved by a method for measuring biomagnetic, in particular, cardiomagnetic, fields by means of at least one antenna made of superconducting material, preferably arranged in a Dewar container, wherein the antenna has at least one first coil for inductive detection of a magnetic field and a second coil, and by means of a SQUID which is inductively coupled with the antenna via the input coil, wherein the SQUID is operated in the relaxation oscillation mode.

Preferably, the method is performed such that an internal unshunted SQUID with hysteresic voltage-current characteristic and two areal superconducting areas connected to one another by two Josephson junctions (tunnel connections) and connected with one another externally by a resistor R and an inductive resistor L, series-connected to the resistor R, are employed and that a bias voltage is supplied to the SQUID such that the relaxation oscillation mode is realized.

Further details and advantages of the invention result from the following purely exemplary and non-limiting description of a few embodiments in connection with the drawing, in which:

	Fig. 1	is a schematic illustration of a magnetograph for performing biomagnetic measurements on patients;
	Fig. 2	is a section of a cryogenic magnetometer embodied according to the invention;
5	Fig. 3	is a schematic circuit diagram of a second-order gradiometer according to the invention with a SQUID that can be operated in RO mode;
	Fig. 4	is a schematic circuit diagram of an electronic measuring device for operating the SQUID in RO mode;
10	Fig. 5	is a SQUID of the washer type in a plan view;
	Fig. 6	is a schematic illustration of the antenna and of a further second-order gradiometer according to the invention with a SQUID that can be operated in the RO mode and is coupled inductively with the antenna;
15	Fig. 7	is a schematic illustration of the Dewar container and gradiometer and measuring electronic device arranged in a magnetically shielded housing;
	Fig. 8	shows the hysteresic voltage-current characteristic of a SQUID to be used according to the invention;
20	Fig. 9	shows the characteristic lines of a SQUID according to the invention wherein the line 1 shows the dependency of the feedback loop amplification coefficient G for an open slew rate

(SR) as a function of the frequency of the measured signal; and

shows the RO frequency dependency of magnetic flux MF wherein the line 1 shows the course without and the line 2 the course with additional positive feedback (APF); 2) and wherein for clarification the circuit diagram of the SQUID APF circuit is inserted into the Figure.

Fig. 1 shows a magnetograph comprising a Dewar container 1 in which the actual measuring device is arranged and which is suspended from a gantry 2. The magnetograph comprises furthermore a frame 3 with a movable support 4, with which the patient 5 to be examined can be positioned underneath the measuring device; a comparison EKG 6; a control unit 7; a personal computer 8; and a connecting cable 9 for connecting the measuring device arranged in the container 1 with the control unit 7.

The gantry 2 and the movable support 4 together make possible the positioning of the patient 5 relative to the measuring device in the desired way. The gantry, support and frame are made of non-magnetic material such as wood or Textolite.

The cryogenic magnetometer illustrated in section in Fig. 2 comprises a magnetically transparent Dewar container 2 which is filled with liquid helium 4 for the purpose of cooling the superconducting components to the required temperature. In this embodiment, the container is made of fiberglass and has a capacity of approximately five liters. An antenna 5 is arranged in the end area 7 of the container facing the magnetic field to be measured; a signal processing unit 3 is positioned in the opposite area forming the head of the container; and the SQUID 1 is arranged in the central area of the container.

20

5

10

15

The antenna 5 forms with its windings 8, 9, and 10 a second-order gradiometer 2 which detects the component d2B/dz2, i.e., the diagonal component of the magnetic gradient sensor. The gradiometer is comprised in the illustrated embodiment of a that is wound, wherein the baseline is 60 mm. The reference coil 8 and the pickup coil 10 are comprised of a single winding while the central reference coil 9 has two windings.

5

10

15

20

25

The gradiometer inductivity as well as the inductivity of the SQUID input coil is 1  $\mu$ H in order to optimize the flux transformation.

In Fig. 3, the core of the measuring device is schematically illustrated which is comprised of a SQUID 3, an input coil 6, a feedback coil 7, and means for operating the SQUID in the RO mode. The DC SQUID is shunted by means of a resistor R 4 and an inductive resistor L 5 series-connected thereto so that an RO generator is formed. The device is surrounded by a superconducting shielding 8 which prevents the penetration of external magnetic disturbances into the SQUID [*Schl?*]. The transformation factor of the device is 10 MHz/ $\Phi_0$ , the dynamic range is 140 dB, the flux resolution is 8  $\mu\Phi_0$ / $\nu$ Hz, the input energy sensitivity is  $\epsilon_{\rm S}$  =10<sup>-30</sup>J/Hz, the sensitivity with respect to the magnetic field is 30 fT/ $\nu$ Hz, and the maximum slew rate is 3·10<sup>6</sup>  $\Phi_0$ /s.

In Fig. 4, a schematic illustration of the measuring electronic device for operating the SQUID in RO mode is illustrated. The core of the system is the RO SQUID which, as illustrated in Fig. 6, is comprised of a SQUID with two superconducting areas shunted by means of a resistor R and an inductive resistor L which are connected in series.

The magnetic field (MAGNETIC FIELD) to be measured is detected by the antenna (ANTENNA) which is coupled inductively with the SQUID.

The SQUID is connected with a bias voltage source (BIAS SOURCE) and an amplifier (PULSE AMPLIFIER). The magnetic flux effects within the SQUID measurable voltage pulses whose frequency depends on the strength of the magnetic flux and which are amplified in the amplifier before they are supplied to a comparator (PULSE COMPARATOR), a former (PULSE FORMER), and an integrator (INTEGRATOR). The integrator is connected via a buffer follower (BUFFER FOLLOWER) with a power supply and control unit (CONTROL UNIT) which, in turn, is directly connected with the integrator. Moreover, the integrator is also connected with the RO-SQUID.

5

10

15

20

25

When the direct current bias voltage is supplied to the RO SQUID, the generation of RO pulses begins whose frequency is determined by a measurable magnetic field. The RO pulses flow through the pulse amplifier, reach the pulse comparator, wherein the background amplitude noise of the pulse amplifier output is cut off and the pulse duration is extended to a value sufficient for the next cascade. After the RO pulses have left the comparator, they reach the pulse former and from there the integrator. The signal exiting the integrator runs through the buffer follower. This electronic signal processing device is arranged in the unit identified at 9 in Fig. 1. Its parameters are: frequency transmission band relative to the 3 dB level: 0+50 kHz; output voltage for 1 flux quantum: 10 V; output voltage for 10 pT of input signal: 80 mV; LFF passage band - 30 Hz (-3 dB level).

The thin film SQUID of the so-called washer type according to Fig. 5 is configured based on the unshunted NbN-NbN $_x$ O $_y$ -Nb Josephson junctions 26 and 28 and comprises two areas 32 and 34 of superconducting material which are connected to one another by the Josephson junctions 26, 28. The larger area 34 of the two areas 32 and 34 has an edge length of approximately 2 mm. The two areas 32 and 34 enclose a surface 40, which is not to scale and which, in reality, is approximately 40 by 40 µm. The characteristic data of this SQUID suitable for the here described application are:  $V_g = 3.8 - 4.0$  mV,  $R_n = 15 - 40$  Ohm,  $R_y/R_n = 12 - 44$ ,  $I_c = 3 - 5$  µA.

Its voltage-current characteristic is schematically illustrated in Fig. 8.

5

10

15

20

In Fig. 6 a second-order gradiometer is illustrated which is comprised, on the one hand, of an antenna, referenced in its entirety at 10, with a pickup coil 12, three bucking coils 14, 16, and 18, and an input coil 20. The antenna is bent from a single niobium wire loop 22. The "baseline" b (the spacing between pickup coil 12 and first bucking coil 14) is approximately 6 cm.

The gradiometer is comprised moreover of a so-called "unshunted" low temperature SQUID 24 with two Josephson junctions 26 and 28 of high capacitance C, wherein the SQUID 24 is inductively coupled with the antenna 10 via the input coil 20. The SQUID is moreover coupled, as is known in the art, with the feedback coil 30. The two superconducting areas 32 and 34 (see Fig. 5) of the SQUID are connected, in addition to the connection by the Josephson junctions, externally via a resistor 36 with value R and a coil 38 with inductivity L, wherein the coil 38 and the resistor 36 are connected in series.

During operation, the SQUID is supplied with a bias current  $I_b$  which satisfies the condition  $I_c < I_b < V_p/R$  wherein  $I_c$  is the critical voltage of a Josephson junction, R is the resistance of the resistor 36, and  $V_p$  is the plasma voltage of a Josephson junction which satisfies the condition  $V_p = V_c \beta^{-1/2}$ , wherein  $V_c = I_c R_c$  with  $V_c$  as the critical voltage,  $I_c$  as the critical current, and  $R_n$  as resistance of a Josephson junction. When the condition  $\tau >> \tau_n$ , wherein  $\tau = L/R$  and  $\tau_n = CR_n$  are satisfied, a relaxation oscillation in the SQUID with the period duration

$$T = T_0 [1 + (\pi/2)(L_c/L)] + (4/\pi + \pi/4)\tau_n$$

results wherein  $T_0 = r \ln \left[ (1 + I_c R/(V_g - RI_b))/(1 - I_c/I_b) \right], L_c = \Phi_c/2\pi I_c, V_g = 4V_c/\pi$ .

Based on the equation for the period duration T, the dependency of the critical

current of the SQUID results which again depends on the measured magnetic flux  $\Phi$  which, as is known in the art, is quantized in units of  $\Phi_0$ . When starting with relaxation oscillations with relatively low frequencies of a few MHz and using the dependency of the RO frequency F on the magnetic flux as a base signal, very good measuring results can be obtained with the gradiometer. In this connection, a working point in the area of the greatest incline dF/d $\Phi$  is selected.

5

10

15

20

25

By means of a negative feedback loop the magnetic field is integrated fixedly into the SQUID interferometer ring which leads to a fixation of the working point at a specified RO frequency.

Fig. 7 is a basic schematic of a Dewar container 44 together with the antenna 10 and SQUID 24 arranged in a magnetically shielded housing 42 expediently of two plastic material shells 42a and 42b, wherein the upper shell 42a can be easily removed so that, if needed, cooling medium, in particular, liquid helium can be filled into the Dewar container.

Housing 42 and Dewar container 44 are lined at their inner sides with aluminum foil 48 and 50, respectively, for magnetic shielding wherein in the housing 42 an opening for the lower area 52 of the Dewar container containing the pickup coil of the antenna is provided and this area of the container is not shielded so that a magnetic field generated by an electric dipole p can be detected by the gradiometer.

The Dewar container is configured such that the spacing between the bottom side of the pickup coil facing the container and the outer side of the container is between approximately 3 and 10 mm and the container has a volume for approximately 6 l cooling medium. When liquid helium is used for cooling, the typical loss rate is approximately 1.2 I helium per day so that with this configuration of the container helium must be refilled only every third day.

In the described way, a system for measuring biomagnetic fields can be configured whose system noise is under 30 fT/ $\sqrt{\rm Hz}$  for a dynamic range of 140 dB and a slew rate of 10<sup>6</sup> O<sub>0</sub>/s.

The data acquired with such a system can be evaluated in very different ways, in particular, can be analyzed with respect to the strength and local position of the sources of the magnetic fields.

5

10

In the context of the principle of the invention, numerous modifications and further developments are possible. Even though the described device has been constructed for measuring biomagnetic fields, it is, of course, also suitable for measuring magnetic fields of a different origin.

#### Claims

 A device for measuring biomagnetic, in particular, cardiomagnetic, fields by means of at least one superconducting quantum interference device (SQUID), characterized in

that the SQUID is a SQUID with hysteresic voltage-current characteristic and

5

10

15

20

that means for operating the SQUID in a relaxation oscillation mode (RO mode) are provided.

- 2. The device according to claim 1, characterized in that the SQUID is a direct-current SQUID (DC SQUID).
- 3. The device according to claim 1 or 2, characterized in that the SQUID has at least two Josephson junctions (tunnel connections).
- 4. The device according to claim 3, characterized in that the at least two Josephson junctions are internally unshunted and are connected by a line with one another.
- 5. The device according to claim 3 or 4, characterized in that the at least two Josephson junctions have such a capacitance C that the voltage-current characteristic of the SQUID has hysteresis.
- 6. The device according to one of the claims 1 to 5, characterized in that the means for operating the SQUID in the relaxation oscillation mode comprise a resistor R and an inductive resistor L which are series-connected to one another.
- 7. The device according to claim 6, wherein the SQUID has two areal superconducting areas connected to one another by the at least two Josephson

junctions (tunnel connections), characterized in that the two superconducting areas, in addition to the connection via the Josephson junctions, are connected with one another by the resistor R and the inductive resistor L.

- 8. The device according to claim 7, characterized in that the greater one of the two superconducting areas has an edge length between 1.5 and 2.5 mm, preferably of approximately 2 mm.
- 9. The device according to one of the claims 7 or 8, characterized in that the surface area enclosed by the two superconducting areas of the SQUID is between 1,200 in 2,000  $\mu$ m<sup>2</sup>, preferably approximately 1,600  $\mu$ m<sup>2</sup>.
- 10. The device according to one of the claims 1 to 9, characterized in that the SQUID is a low-temperature SQUID.

5

- 11. The device according to one of the claims 1 to 10, characterized in that the SQUID is a SQUID of a washer configuration.
- 12. The device according to one of the claims 1 to 11, characterized in that the at least one SQUID is coupled inductively by means of an input coil with at least one antenna.
- 13. The device according to claim 12, characterized in that the antenna is comprised of superconducting material and has at least one first coil (pickup coil) for inductive detection of a magnetic field and a second coil (input coil).
- 20 14. The device according to one of the claims 12 or 13, characterized in that the antenna is a gradiometer antenna with a pickup coil and at least one bucking coil, in particular, a symmetric axial second-order gradiometer antenna with a pickup coil and three bucking coils.

- 15. The device according to claim 14, characterized in that the baseline of the gradiometer antenna is between 5 and 7 cm, preferably approximately 6 cm.
- 16. The device according to one of the claims 14 or 15, characterized in that means for mechanically compensating (balancing) the gradiometer, in particular, a mechanism for exact positioning of one or several superconducting objects in the vicinity of the pickup coil and or the bucking coil

5

15

- 17. The device according to one of the claims 13 to 16, characterized in that the diameter of the pickup coil and of the optionally present bucking coil(s) is between 1.5 and 2.9 cm, preferably approximately 2.2 cm.
- 18. The device according to one of the claims 13 to 17, characterized in that the pickup coil and the optionally present bucking coil(s) each comprise only one winding.
  - 19. The device according to one of the claims 12 to 18, characterized in that the antenna is comprised of wire, in particular, niobium wire or niobium nitrate wire, with a diameter between approximately 30 and 60 µm.
  - 20. The device according to one of the claims 12 to 19, characterized in that the input coil has approximately 20 to 40 windings.
  - 21. The device according to one of the claims 12 to 20, characterized in that a lens for bundling the magnetic field lines, in particular, in the form of a thin foil of superconducting material, is provided between input coil and SQUID.
  - 22. The device according to one of the claims 1 to 21, characterized in that the SQUID is arranged in a Dewar container.

- 23. The device according to one of the claims 13 to 18 and claim 22, characterized in that the Dewar container with exception of an area underneath the pickup coil is provided with a magnetic shielding, in particular, is lined with aluminum foil.
- The device according to claim 23, characterized in that the Dewar container is configured such that the spacing between the bottom side of the pickup coil facing the container and the outer side of the container is between approximately 3 and approximately 10 mm.
  - 25. The device according to claim 23 or 24, characterized in that a magnetically shielded housing, in particular, lined with aluminum foil, is provided which surrounds the Dewar container and the important sensitive parts of the electronic device required for operating the SQUID and has an opening for the area of the Dewar container containing the pickup coil.

10

- 26. The device according to one of the claims 22 to 25, characterized in that the Dewar container has a cooling medium volume in the range of a few liters, in particular, between 2.5 and 10 l.
  - 27. The device according to one of the claims 1 to 26, in particular, for detecting cardiomagnetic fields, characterized in that only one or a few, preferably four to nine, SQUID(s) having an antenna, respectively, are provided.
- 28. The device according to one of the claims 1 to 27, with at least one pickup coil, in particular, for determining cardiomagnetic fields, characterized in that a movable table for positioning an object to be examined relative to the pickup coil(s) is provided.
  - 29. The device according to claim 28, characterized in that the table is comprised

of non-conducting material, in particular, of wood and/or plastic material.

- 30. The device according to one of the claims 28 or 29, characterized in that a locking and guiding mechanism for moving the table along predetermined paths and for locking the table in certain positions is provided.
- 31. The device according to one of the claims 28 to 30, characterized in that means for automatically positioning the table relative to the pickup coil(s) is provided.

5

10

15

- 32. The device according to claim 31, characterized in that the means for automatically positioning the table relative to the pickup coil(s) are hydraulic and/or mechanical means, in particular, comprising one or several spindle drives.
- 33. The device according to one of the claims 28 to 32, characterized in that the movable table and the pickup coil(s) are embodied such that, when measuring magnetic fields at different locations of the object, the object is moved relative to the pickup coil(s) by moving the table while maintaining the absolute position of the pickup coil(s).
- 34. The device according to one of the claims 1 to 33, characterized in that a measuring or evaluation electronic device is provided for automatic consideration of disturbances that can be derived from the periodic current-flux characteristics for switched-off feedback, in particular, for automatic discarding of measured values recorded during the occurrence of disturbances.
- 35. A method for measuring biomagnetic, in particular, cardiomagnetic fields by means of at least one antenna of superconducting material arranged in the Dewar container, wherein the antenna comprises at least one first coil (pickup coil) for inductive detection of a magnetic field and a second coil (input coil), and by means

of a SQUID inductively coupled to the antenna in the Dewar container via the input coil,

characterized in

15

20

25

that the SQUID is operated in the relaxation oscillation mode.

- 5 36. The method according to claim 35, wherein an internally unshunted SQUID with hysteresic voltage-current characteristic and with two areal superconducting areas connected to one another by two Josephson junctions (tunnel connections), which are externally connected to one another by means of a resistor R and an inductive resistor L series-connected to the resistor R, is used, characterized in that a bias voltage is applied such to the SQUID that the relaxation oscillation mode is realized.
  - 37. The method according to claim 35 or 36, characterized in that, before measuring biomagnetic fields, information in regard to the noise present at the installation site, in particular, information in regard to the causes of the noise, is obtained from the periodic current-flux characteristics of the SQUID with the feedback being switched off.
  - 38. The method according to one of the claims 35 to 37, characterized in that, before measuring biomagnetic fields, the SQUID is tested in regard to its proper function and quality by observing the periodic current-flux characteristic of the SQUID with the feedback being switched off.
  - 39. The method according to one of the claims 35 to 38, characterized in that certain disturbances of the measurement are automatically taken into consideration, in particular, in that the measured values recorded at the time of occurrence of the disturbances are automatically discarded.
  - 40. The method according to one of the claims 35 to 39, wherein the antenna is

configured as a gradiometer, characterized in that the gradiometer is mechanically compensated (balanced), in particular, by positioning one or several superconducting objects in the vicinity of the pickup coil and of the bucking coil(s).

41. The method according to one of the claims 35 to 40, in particular, for detecting cardiomagnetic fields, characterized in that the object to be examined is moved into one or several different positions relative to the pickup coil(s).

5

- 42. The method according to claim 41, characterized in that the absolute position of the pickup coil(s) is not changed when performing the relative movement of the object to be examined and the pickup coil(s).
- 10 43. The method according to claim 41 or 42 for detecting cardiomagnetic fields, characterized in that the fields are measured on 36 points of a rectangular grid at a 4 cm spacing, respectively, to the neighboring points.
  - 44. The use of a device according to one of the claims 1 to 34 for detecting cardiomagnetic fields, in particular, in rooms not shielded against external electromagnetic fields.





#### (12) NACH DEM VERTRAG ÜBER DIE INTERNATIONALE ZUSAMMENARBEIT AUF DEM GEBIET DES PATENTWESENS (PCT) VERÖFFENTLICHTE INTERNATIONALE ANMELDUNG

(19) Weltorganisation für geistiges Eigentum Internationales Büro



# THE REPORT OF THE PARTY OF THE P

(43) Internationales Veröffentlichungsdatum
1. Februar 2001 (01.02.2001)

**PCT** 

# (10) Internationale Veröffentlichungsnummer WO 01/06907 A2

(51) Internationale Patentklassifikation7:

----

A61B

(21) Internationales Aktenzeichen:

PCT/DE00/02472

(22) Internationales Anmeldedatum:

27. Juli 2000 (27.07.2000)

(25) Einreichungssprache:

Deutsch

(26) Veröffentlichungssprache:

Deutsch

(30) Angaben zur Priorität: 199 34 476.0 27. Juli 1999 (27.

27. Juli 1999 (27.07.1999) DE

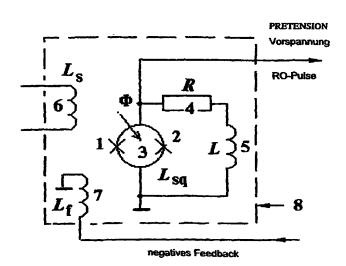
(71) Anmelder (für alle Bestimmungsstaaten mit Ausnahme von US): SQUID AG [DE/DE]; Kruppstrasse 94, D-45145 Essen (DE).

- (72) Erfinder; und
- (75) Erfinder/Anmelder (nur für US): STEINBERG, Fritz [DE/DE]; Mausegattstrasse 29, D-45472 Mülheim an der Ruhr (DE). SOSNITZKY, Volodymyr [UA/DE]; Kruppstrasse 94, D-45145 Essen (DE).
- (74) Anwalt: KREUTZER, Ulrich; Kruppstrasse 92, D-45145 Essen (DE).
- (81) Bestimmungsstaaten (national): AE, AG, AL, AM, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CN, CR, CU, CZ, DM, DZ, EE, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

[Fortsetzung auf der nachsten Seite]

(54) Title: METHOD AND DEVICE FOR MEASURING BIOMAGNETIC AND IN PARTICULAR CARDIOMAGNETIC FIELDS

(54) Bezeichnung: VERFAHREN UND VORRICHTUNG ZUR MESSUNG BIOMAGNETISCHER, INSBESONDERE KARDI-OMAGNETISCHER FELDER



(57) Abstract: The present invention relates to a method and a device for measuring biomagnetic and in particular cardiomagnetic fields. The problem of known methods and devices lies in that the apparatus used have costly maintenance and in that significant measuring results can only be obtained in magnetically sheltered premises. The device and the method of the present invention allow for the detection of biomagnetic fields using particularly simple means even in non-magnetically sheltered premises. To this end, the device includes at least one superconducting quantum interferometer (SQUID) and is characterised in that said interferometer has a characteristic intensity-voltage curve which is hysteretic and in that means are provided for operating said interferometer according to a relaxation oscillation (RO) mode.

[Fortsetzung auf der nächsten Seite]



01/06907

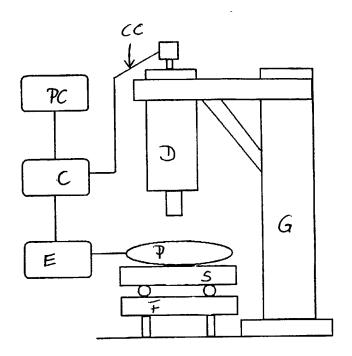


Fig. 1

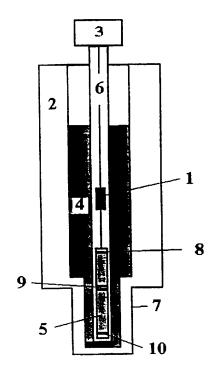
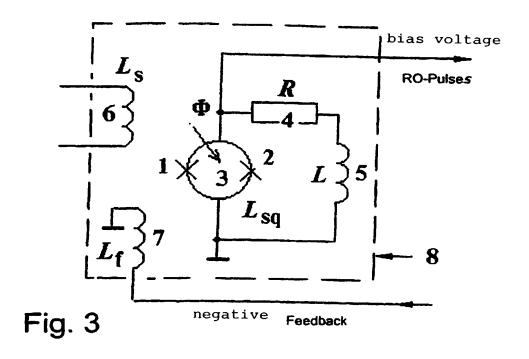
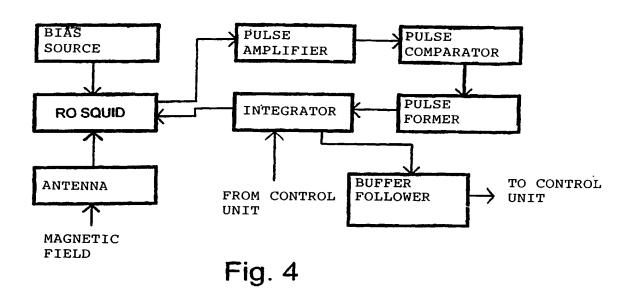


Fig. 2





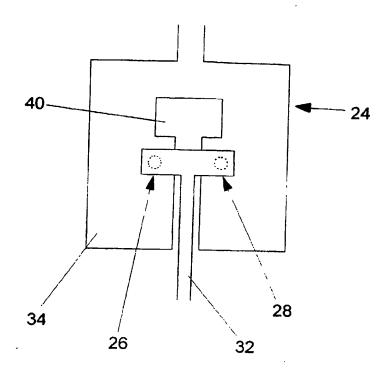
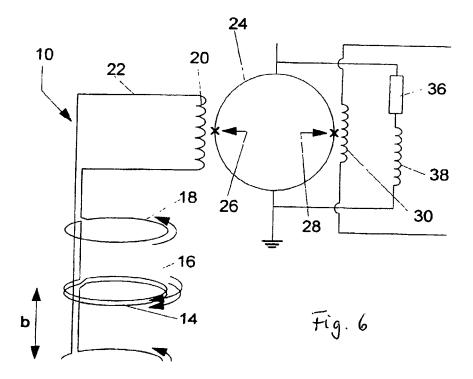


Fig. 5



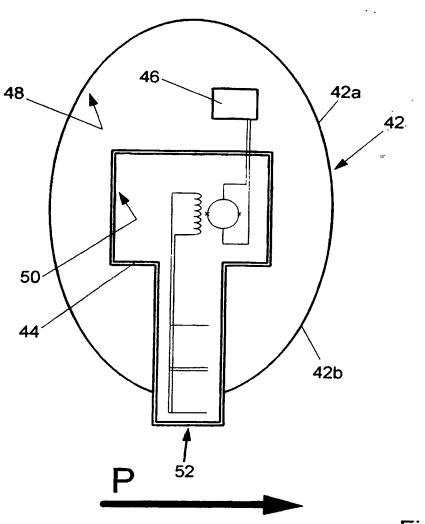


Fig. 7

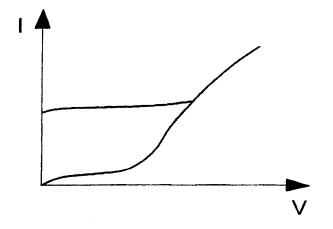
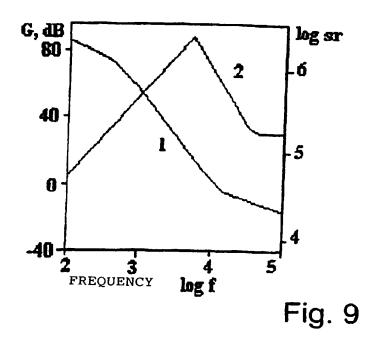


Fig. 8



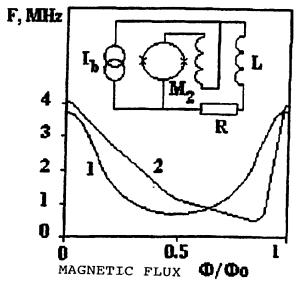


Fig. 10

#### Attorney Docket No. S04P02US

#### **DECLARATION FOR UTILITY OR DESIGN PATENT APPLICATION (37 CFR 1.63)**

#### As a below named inventor, I hereby declare that:

... لسر خ . . .

the specification of which

0

My residence, post office address and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought of the invention entitled:

### Method and Device for Measuring Biomagnetic and in Particular Cardiomagnetic Fields

[ ]	is attached hereto; or	
[ X]	was filed on 1/28/2002	
	as US Application Ser. No. 10/049,247	
	or PCT Application No.	
	and was sevended on	

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above.

Lacknowledge the duty to disclose information which is material to patentability as defined in 37 CFR 1.56.

I hereby claim foreign priority benefits under Title 35 U.S.C. 119 (a)-(d) or 365(b) of any foreign application(s) for patent or inventor's certificate, or 365(b) of any PCT international application which designated at least one country other than the United States of America, listed below and have also identified below, by checking the box, any foreign application for patent or inventor's certificate, or any PCT international application having a filing date before that of the application on which priority is claimed.

Prior Foreign	Country	Foreign Filing Date	Priority Claimed	
Application Ser. No		(Month/Day/Year)	Yes	No
19934476.0	Germany	7/27/1999	Х	
		·		

#### Attorney Docket No. S04P02US

I hereby claim the benefit under 35 U.S.C. § 119(e) of any United States provisional application(s) listed below:

Application No.	Filing Date (Month/Day/Year)		

I hereby claim the benefit under Title 35 U.S.C. 120 of any United States application(s), or 365(c) of any PCT international application designating the United States of America, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT international application in the manner provided by the first paragraph of 35 U.S.C. 112, I acknowledge the duty to disclose information which is material to patentability as defined in 37 CFR 1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application:

U.S. Parent Application or PCT Parent No.	Parent Filing Date (Month/Day/Year)	Parent Patent No.
	_	

As a named inventor, I hereby appoint the following registered practitioner to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith:

GUDRUN E. HUCKETT, REGISTRATION NO. 35,747

Direct all correspondence and communications to the correspondence address and telephone and fax numbers below:

GUDRUN E. HUCKETT, PATENT AGENT

P.O. BOX 3187

ALBUQUERQUE, NM 87190-3187

Telephone:

(505) 266-2138

Fax:

(505) 266-2138.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these

## Attorney Docket No. S04P02US

statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. 1001 and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

ru	Full name of sole or first inventor:	Fritz Steinberg
	Inventor's signature:	Date: 09-04-02
	Residence: Mausegattstr. 29, 45472 Müll	neim an der Ruhr, Germany
	Citizenship: Germany	DEV
	Post Office Address: same as above	7- /
	Full name of second inventor, if any:	Volodymyr Sosnitzky
ı	Inventor's signature:	Date: 09.04.02
	Residence: Kruppstr. 94, 45145 Essen, G	ermany
	Citizenship: Ukraine	DEX
	Post Office Address: same as above	,
	Full name of third inventor, if any:	
	nventor's signature:	Date:
	Residence:	
	Citizenship:	
	Post Office Address:	
	Full name of fourth inventor, if any:	
	nventor's signature:	Date:
	Residence:	
	Citizenship:	
1	Post Office Address:	
į	full name of fifth inventor, if any:	
1	nventor's signature:	Date:
F	Residence:	_
(	Citizenship:	
•	Post Office Address:	

ō